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Ten-year outcomes of antiretroviral therapy: a retrospective cohort study in Tshwane district, South Africa

Kateko Mhlongo[1], Murray Louw[2] and Sanele Ngcobo[2*]

Abstract

Background South Africa continues to face one of the world's highest HIV burdens, with 7.7 million people living with HIV (PLWHIV) in 2023. Despite progress toward UNAIDS 95–95–95 targets, challenges in long-term retention and treatment outcomes persist. This study aimed to evaluate 10-year antiretroviral therapy (ART) outcomes among PLWHIV initiated on treatment in 2013 within Tshwane District, South Africa.

Methods Retrospective cohort using Tier.Net data from 1,337 adults across 10 randomly selected facilities (clinics and community health centres [CHCs]). Outcomes were retention, loss to follow-up (LTFU), mortality, viral suppression, and CD4 recovery. We used Kaplan–Meier methods and multivariable models (Cox for LTFU and mortality, logistic for viral suppression, linear for CD4 change). Mortality analyses were limited to participants with complete ascertainment ($n = 640$).

Results At 10 years, 47.7% were retained, 30.4% LTFU, 20.1% transferred out, and 3.3% died. Attrition was steepest early and most pronounced among 18–24-year-olds. Advanced WHO stage strongly predicted death (Stage III/IV vs. I/II: aHR 3.06, 95% CI 1.26–7.44), and younger age was protective (≤ 34 vs. > 34 years: aHR 0.28, 95% CI 0.09–0.86). Care at CHCs was associated with lower mortality (aHR 0.33, 95% CI 0.13–0.83) and greater CD4 gains (clinic care: −74.35 cells/μL vs. CHCs; $p < 0.001$). Female sex was associated with larger CD4 recovery (+ 90.06 cells/μL vs. males; $p < 0.001$). Only baseline CD4 > 200 cells/μL independently predicted viral suppression (aOR for being suppressed ≈ 1.89, derived from aOR 0.53 for non-suppression; $p < 0.001$). No baseline covariates were significant predictors of time to LTFU (clinic type borderline: HR 0.80, $p = 0.086$).

Conclusion A decade after initiation, fewer than half remained in care. Mortality clustered among older adults and those presenting with advanced disease, while CHC-based care conferred survival and immunologic advantages. Programme priorities should include earlier diagnosis and ART start, youth-friendly retention strategies, and scaling CHC-style differentiated service delivery to improve long-term outcomes.

Keywords HIV, Antiretroviral therapy, Retention in care, Mortality, Viral suppression, South africa, Tshwane, Long-term outcomes

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Introduction

South Africa remains at the epicentre of the global HIV epidemic, with an estimated 7.7 million people living with HIV (PLWHIV) in 2023 [1]. That year alone, approximately 160,000 new infections were reported, reflecting ongoing transmission despite significant progress in antiretroviral therapy (ART) coverage [1]. In line with the UNAIDS Fast-Track strategy, initially framed as the "90–90–90" targets and later updated to "95–95–95," South Africa has achieved 94% of PLWHIV knowing their HIV status, 74% on treatment, and 69% achieving viral suppression [1]. While these figures demonstrate substantial public health gains, they also reveal critical gaps, particularly in the treatment and viral suppression cascade. Effective and timely linkage to ART is the cornerstone of HIV care and is strongly associated with reduced morbidity, mortality, and transmission [2]. However, long-term retention in care remains one of the most significant challenges facing HIV programs, particularly in resource-limited settings. Loss to follow-up (LTF), suboptimal adherence, and late initiation continue to hinder the full potential of ART in South Africa [3, 4]. Retention is influenced by a complex interplay of factors, including socio-economic challenges, healthcare system barriers, and individual-level determinants such as age, gender, and baseline clinical status [5].

Notably, men are consistently less likely to remain engaged in care, initiate treatment earlier, or achieve viral suppression compared to women [6, 7]. Younger individuals also face disproportionate challenges in staying in care, with high rates of disengagement attributed to stigma, mobility, and competing social priorities [8]. Understanding the long-term outcomes of ART is essential for identifying programmatic gaps and designing interventions to improve care continuity. Despite national ART scale-up since the early 2000s, few studies in South Africa have examined patient trajectories over a full decade of treatment. Evaluating such long-term outcomes is especially critical in urban settings like Tshwane District, which face diverse population needs and service delivery constraints.

This study aimed to assess 10-year ART outcomes specifically retention in care, mortality, viral suppression, and demographic and clinical predictors among adults initiated on treatment in 2013 across selected clinics and community health centres (CHCs) in Tshwane. By leveraging routine programmatic data from Tier.Net, we seek to contribute evidence to inform targeted strategies that support sustained engagement in HIV care and help achieve the final leg of the UNAIDS 95–95–95 goals.

Methodology

Study setting

This study was conducted in the Tshwane district, located in Gauteng Province, South Africa. Secondary data from the Tshwane district were utilized. A total of 10 clinics and CHCs were randomly selected within the Tshwane district to form the study setting. Facilities were stratified by type (clinics vs. CHCs). A complete list of eligible facilities providing ART services in 2013 was compiled from the Tier.Net database, and simple random sampling was then applied within each stratum using a random number generator to select the required number of clinics and CHCs. These facilities were chosen to address the research objective of assessing the treatment outcomes over 10 years period from 2013 to 2023 of patients initiated on ART in the year 2013.

Study design

A retrospective cohort study was employed to evaluate the treatment outcomes of patients initiated on ART in the Tshwane district in 2013. The study utilized retrospective data extracted from Tier.Net, a nationally implemented electronic patient management system. Tier.Net is designed to support the monitoring and evaluation of HIV care and treatment programs in public health facilities across South Africa. It collects and manages comprehensive data on patients receiving HIV care, including clinic visit records, laboratory results (e.g., CD4 counts, viral load measurements, tuberculosis results), ART dispensing records, and patient outcomes such as transfers out, loss to follow-up, mortality, and transfers in. Tier.Net is widely used in the country and serves as a critical tool for managing patient data, identifying gaps in care, and improving health outcomes within the national HIV response framework.

Population study

The study population comprised people living with HIV (PLWHIV) aged 18 years and older who were initiated on ART in the Tshwane district in 2013. Inclusion criteria were PLWHIV aged ≥ 18 years, initiated on ART, and captured in Tier.Net between January 1, 2013, and December 31, 2013. Exclusion criteria included individuals diagnosed in 2013 but not initiated on ART in the same year and those initiated on ART in 2013 but not captured in Tier.Net.

Data collection

Data for this study were extracted from Tier.Net, adhering to the inclusion and exclusion criteria defined for the study population. The extracted data included variables such as ART initiation dates, baseline WHO clinical stages, baseline CD4 counts, ART regimens at initiation, treatment duration, occurrences of tuberculosis (TB)

infections, ART regimen changes or switches, and viral suppression rates. Data were directly extracted from Tier.Net int into the UP Qualtrics platform by a research assistant who had signed confidentiality agreements and subsequently imported into an SPSS database for statistical analysis. Only de-identified data were exported, with no patient-identifiable information included in the dataset. The researcher conducted data verification, assessed completeness, and consistency.

Data analysis

The statistical analysis aimed to assess demographic and clinical characteristics, as well as outcomes related to retention to care, mortality, and viral suppression. Data were analyzed using IBM SPSS Statistics V.29. A two-step approach was employed, starting with descriptive statistics followed by inferential analyses to explore associations and predictors of key outcomes. Descriptive statistics were used to summarize participant characteristics, with categorical variables presented as frequencies and percentages, and continuous variables were summarized using means and standard deviations (SDs).

For time-to-event outcomes, we modelled (i) loss to follow-up (LTFU) and (ii) mortality from ART initiation using Cox proportional hazards regression, reporting adjusted hazard ratios (aHRs) with 95% CIs (Tables 3 and 4). Analyses used the covariates applied throughout the results: sex (female vs. male), age group (≤ 34 vs. > 34 years), baseline CD4 (≤ 200 vs. > 200 cells/μL), WHO clinical stage (I–II vs. III–IV), and clinic type (clinic vs. CHC). Mortality analyses were performed in the subset with available mortality ascertainment ($n = 640$), as reflected in the results tables. This analysis was restricted to participants whose final outcome was either died or retained in care; individuals who transferred out or LTFU during follow-up were excluded. LTFU was defined as ≥ 90 days overdue for a scheduled clinic visit or ART pickup. For viral load (VL) suppression, we fitted a multivariable logistic regression with the outcome coded as not suppressed (event), and suppression defined as VL < 50 copies/mL at the last measurement. We report adjusted odds ratios (aORs) with 95% CIs, alongside the corresponding crude distributions. The covariates listed above were included in the model. For immune recovery, we analysed change in CD4 (cells/μL) as a continuous outcome using multiple linear regression, where change was defined as last available CD4 minus baseline CD4. Results are presented as adjusted mean differences with 95% CIs.

Missing data were handled by available-case descriptives and complete-case modelling. For Table 1, percentages were calculated among participants with non-missing data for each variable (e.g., clinic type $N = 1{,}290$; baseline CD4 category $N = 1{,}117$; WHO stage $N = 1{,}201$). For multivariable analyses (Cox models for LTFU and mortality; logistic regression for viral load; linear regression for CD4 change), we used listwise deletion—participants with missing values in the outcome or any model covariate were excluded from that specific model; the analytic N is reported in each table. Mortality analyses were restricted to the subset with complete mortality ascertainment ($n = 640$). No imputation was performed.

Table 1 Baseline demographics and clinical characteristics by gender

Characteristic	Category	*n*	%	Mean (SD)
Age group ($N = 1{,}337$)	≤ 34 years	669	50.0	—
	> 34 years	668	50.0	—
Age at ART start (years)	—	—	—	36.10 (9.76)
Sex ($N = 1{,}337$)	Male	452	33.8	—
	Female	885	66.2	—
Clinic type ($N = 1{,}290$)	Clinic	849	65.8	—
	CHC	441	34.2	—
Facility ($N = 1{,}290$)	Eersterust CHC	143	11.1	—
	Lotus Garden Clinic	140	10.9	—
	Folang Clinic	141	10.9	—
	Atteridgeville Clinic	143	11.1	—
	Danville Clinic	141	10.9	—
	Laudium CHC	155	12.0	—
	Stanza Bopape CHC	143	11.1	—
	Bophelong Clinic	142	11.0	—
	FF Ribeiro Clinic	142	11.0	—
Baseline CD4 (cells/μL)	—	—	—	225.23 (167.14)
Baseline CD4 category ($N = 1{,}117$)	≤ 200 cells/μL	525	47.0	—
	> 200 cells/μL	592	53.0	—
WHO clinical stage at ART start ($N = 1{,}201$)	Stage I	715	59.5	—
	Stage II	211	17.6	—
	Stage III	229	19.1	—
	Stage IV	46	3.8	—

Ethical consideration

This study was approved by the University of Pretoria Faculty of Health Sciences Research Committee (Ethics number: 342/2024) and the Tshwane Health Research Committee. A waiver of informed consent was granted as secondary data was used.

Table 2 Multiple linear regression predicting change in CD4 count

Variable	Group	Mean (SD) cells/μL	*n*	B (95% CI)	*p*-value
Age	≤ 34 years (ref)	267.74 (255.58)	669	—	—
	> 34 years	261.06 (228.93)	668	4.79 (-32.38, 41.96)	0.800
Clinic type	CHC (ref)	301.07 (254.03)	441	—	—
	Clinic	242.44 (233.16)	849	-74.35 (-112.17, -36.53)	< 0.001
Gender	Male (ref)	209.57 (188.44)	452	—	—
	Female	292.86 (261.11)	885	90.06 (50.94, 129.18)	< 0.001
WHO Stage	Stage I & II (ref)	263.85 (252.91)	926	—	—
	Stage III & IV	262.03 (202.83)	275	9.49 (-31.46, 50.43)	0.649

Table 3 Multivariable Cox regression of baseline factors associated with time to loss to follow-up (LTFU)

Variable	Retained in care *n* (%)	LTFU *n* (%)	HR (95% CI)	*p*-value
Sex				
Male (Ref)	196 (57.8)	143 (42.2)	1.00	—
Female	403 (62.8)	239 (37.2)	1.04 (0.81–1.35)	0.756
Clinic type				
Clinic (Ref)	372 (63.6)	213 (36.4)	1.00	—
CHC	210 (58.2)	151 (41.8)	0.80 (0.62–1.03)	0.086
Baseline CD4				
< threshold (Ref)	226 (59.2)	156 (40.8)	1.00	—
≥ threshold	253 (59.0)	176 (41.0)	0.91 (0.71–1.16)	0.450
Age				
≤ 34 years (Ref)	280 (56.2)	218 (43.8)	1.00	—
> 34 years	319 (66.0)	164 (34.0)	1.05 (0.82–1.34)	0.703
WHO stage at ART start				
Stage I–II (Ref)	423 (61.9)	260 (38.1)	1.00	—
Stage III–IV	115 (61.2)	73 (38.8)	0.89 (0.67–1.19)	0.435

Results

At ART initiation, the cohort ($N = 1{,}337$) had a mean age of 36.1 years (SD 9.76), with age groups evenly split (≤ 34 vs. > 34: 50.0%/50.0%) and 66.2% female. Clinic type was available for 1,290 participants; roughly two-thirds received care at clinics (65.8%) and one-third at CHCs (34.2%), with a fairly even spread across individual facilities. Baseline immunologic status was low overall (mean CD4 225 cells/μL, SD 167); among 1,117 with categorized values, 47.0% had CD4 ≤ 200 cells/μL and 53.0% >200 cells/μL. Clinical stage at ART start was available for 1,201 participants; most were WHO Stage I–II (77.1%), with 22.9% at Stage III–IV.

Multiple linear regression predicting change in CD4 count

A multiple linear regression model was used to examine the association between selected baseline characteristics and the change in CD4 count, calculated as the difference between the most recent CD4 measurement during follow-up and the baseline CD4 count at ART initiation. After adjusting for all covariates, clinic type and gender were significantly associated with CD4 change (Table 2). Participants receiving care at CHCs had a higher mean CD4 change (301.07 cells/μL, SD 254.03) than those attending clinics (242.44 cells/μL, SD 233.16). Clinic attendance was associated with a 74.35 cells/μL lower mean CD4 change compared to CHCs (95% CI: −112.17 to −36.53; $p < 0.001$). Female participants had a higher mean CD4 change (292.86 cells/μL, SD 261.11) compared to males (209.57 cells/μL, SD 188.44), with an adjusted mean difference of 90.06 cells/μL (95% CI: 50.94 to 129.18; $p < 0.001$).

In contrast, age (> 34 years vs. ≤34 years) and WHO clinical stage (III & IV vs. I & II) at ART initiation were not significantly associated with CD4 change. For age, the adjusted mean difference was 4.79 cells/μL (95% CI: −32.38 to 41.96; $p = 0.800$), and for WHO stage, it was 9.49 cells/μL (95% CI: −31.46 to 50.43; $p = 0.649$) Table 2.

A detailed breakdown of last available CD4 counts, CD4 changes, and participant counts by year (2013–2023) is provided in Supplementary Table S1. This descriptive table provides context for the regression analysis, illustrating the distribution of follow-up CD4 measurements over time and the progressive increase in mean CD4 counts in line with national HIV treatment guidelines.

Factors associated with loss to Follow-Up

A multivariable Cox proportional hazards regression was conducted to identify factors associated with time to loss to follow-up (LTFU) among patients on ART. None of the assessed variables reached statistical significance in predicting LTFU. Clinic type approached significance, with participants receiving care at CHCs having a 20% lower hazard of being retained in care compared to those at clinics (HR = 0.80, 95% CI: 0.62–1.03, $p = 0.086$). Female sex (HR = 1.04, 95% CI: 0.81–1.35, $p = 0.756$), higher baseline CD4 count (HR = 0.91, 95% CI: 0.71–1.16, $p = 0.450$), older age (HR = 1.05, 95% CI: 0.82–1.34, $p = 0.703$), and WHO stage III–IV at ART initiation (HR = 0.89, 95% CI: 0.67–1.19, $p = 0.435$) were not significantly associated with time to LTFU.

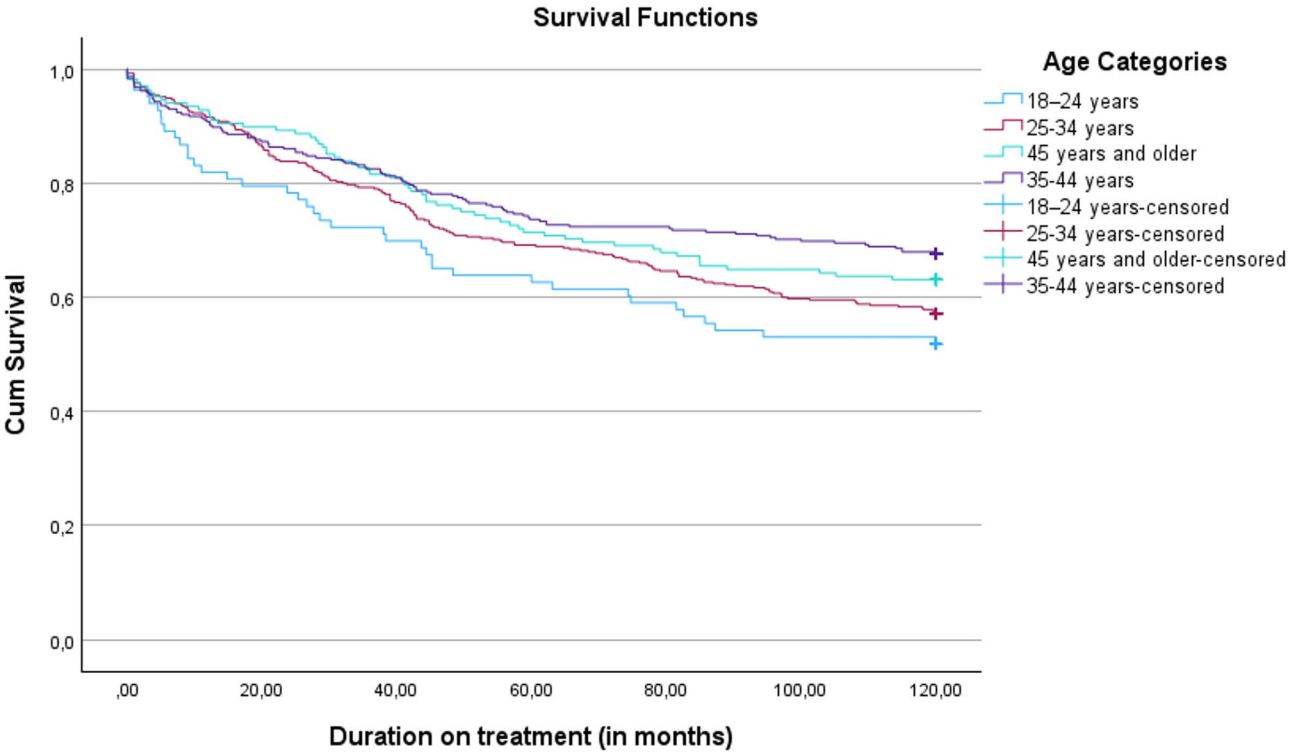

Fig. 1 Kaplan–Meier survival curves showing cumulative loss to follow-up by age category over 120 months of follow-up

Table 4 Mortality distribution and adjusted hazard ratios from Cox proportional hazards regression among ART patients

Predictor	Alive, *n* (%)	Died, *n* (%)	aHR (95% CI)	*p*-value
Sex				
Male	196 (89.5)	23 (10.5)	1.00 (ref)	—
Female	403 (95.7)	18 (4.3)	1.08 (0.49–2.38)	0.853
WHO Stage				
Stage I & II	423 (96.1)	17 (3.9)	1.00 (ref)	—
Stage III & IV	115 (85.2)	20 (14.8)	3.06 (1.26–7.44)	0.013
Age group				
≤ 34 years	280 (96.2)	11 (3.8)	0.28 (0.09–0.86)	0.027
> 34 years	319 (91.4)	30 (8.6)	1.00 (ref)	—
Clinic type				
CHC	210 (95.5)	10 (4.5)	0.33 (0.13–0.83)	0.019
Clinic	372 (92.8)	29 (7.2)	1.00 (ref)	—
Baseline CD4				
≤ 200 cells/μL	226 (90.8)	23 (9.2)	0.91 (0.41–2.01)	0.807
> 200 cells/μL	253 (94.4)	15 (5.6)	1.00 (ref)	—

Kaplan–Meier analysis demonstrated a progressive increase in loss to follow-up across all age categories, with the steepest decline in retention observed among patients aged 18–24 years (Fig. 1). In contrast, older age groups, particularly those aged 35–44 years and ≥ 45 years, maintained comparatively higher retention over the follow-up period.

Mortality and predictors of death

Over the 10-year follow-up period, 41 deaths were recorded among 640 patients with complete mortality data. In the multivariable Cox proportional hazards regression (Table 4), age, WHO stage, and clinic type were significantly associated with mortality. Patients aged ≤ 34 years had a 72% lower hazard of death compared to those > 34 years (aHR = 0.28; 95% CI: 0.09–0.86; $p = 0.027$). Receiving care at a CHC was associated with a 67% lower hazard of death compared to clinic (aHR = 0.33; 95% CI: 0.13–0.83; $p = 0.019$). In contrast, patients presenting with WHO Stage III or IV disease had a threefold higher hazard of death compared to those in Stage I or II (aHR = 3.06; 95% CI: 1.26–7.44; $p = 0.013$). Sex and baseline CD4 count were not significantly associated with mortality.

Kaplan–Meier survival analysis demonstrated significantly lower survival among patients with WHO Stage III and IV disease compared to those in Stages I and II (Fig. 1). The median survival was not reached for any group during the follow-up period; however, patients with advanced stages showed earlier and steeper declines in survival probability Fig. 2.

Viral load

A multivariable logistic regression model was used to examine the association between selected baseline characteristics and having a suppressed last viral load (VL < 50

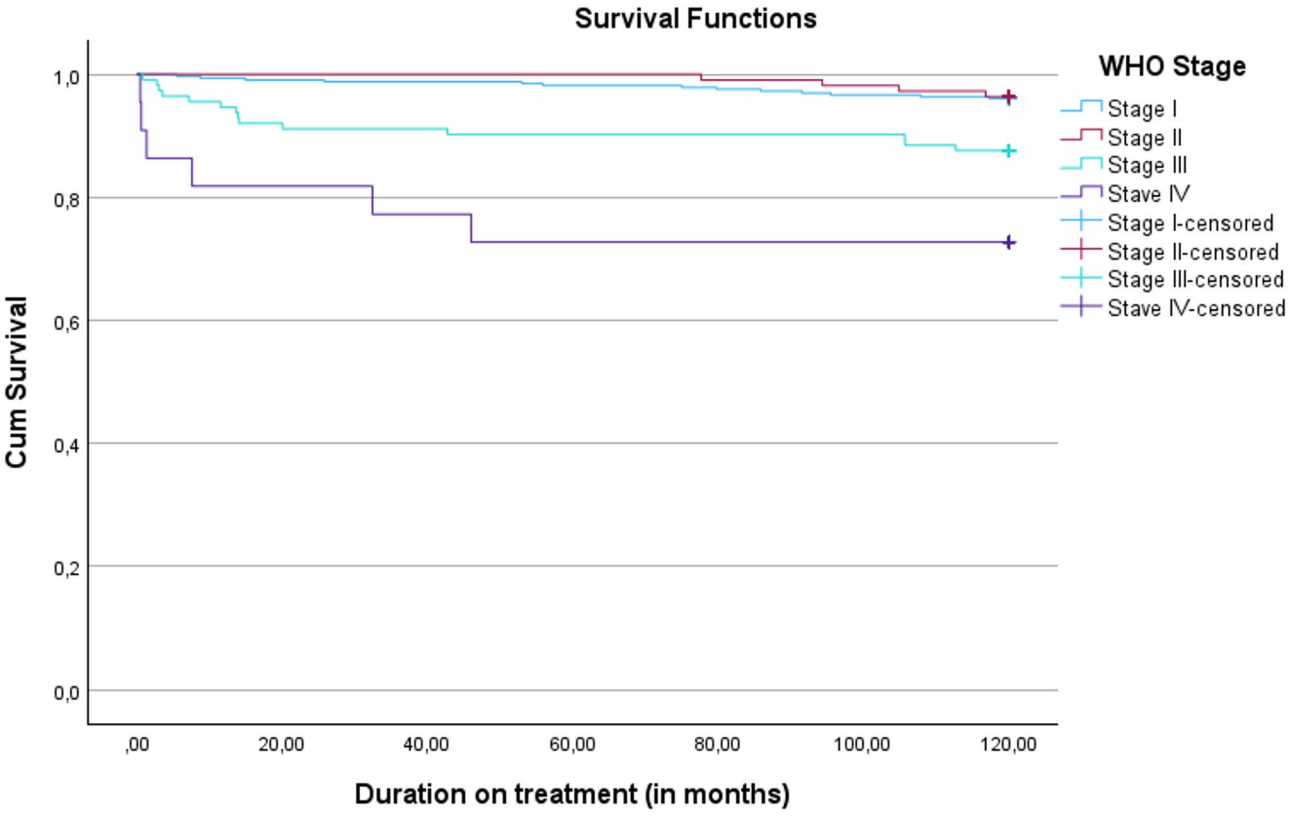

Fig. 2 Kaplan–Meier survival curves for mortality by WHO clinical stage

Table 5 Viral load outcome by baseline characteristics with adjusted odds ratios (multivariable logistic regression)

Variable & category (Ref)	Suppressed *n* (%) < 50 copies/mL	Not suppressed *n* (%)VL ≥ 50	aOR (95% CI)	*p*-value
Clinic type				
Clinic	432 (57.3)	322 (42.7)	1.00	—
CHC	190 (54.6)	158 (45.4)	0.92 (0.68–1.24)	0.587
Age group				
≤ 34 years	309 (55.7)	246 (44.3)	1.00	—
> 34 years	325 (56.2)	253 (43.8)	0.82 (0.62–1.09)	0.164
Baseline CD4 (cells/μL)				
≤ 200	206 (46.1)	241 (53.9)	1.00	—
> 200	318 (61.3)	201 (38.7)	**0.53 (0.40–0.70)**	**< 0.001**
Sex				
Male	193 (50.9)	186 (49.1)	1.00	—
Female	441 (58.5)	313 (41.5)	0.75 (0.55–1.01)	0.055
WHO stage at ART start				
Stage I–II	452 (57.2)	338 (42.8)	1.00	—
Stage III–IV	123 (52.3)	112 (47.7)	0.93 (0.67–1.28)	0.645

copies/mL). Descriptive proportions and adjusted estimates are reported (Table 5). After adjusting for all covariates, baseline CD4 > 200 cells/μL was the only factor independently associated with the VL outcome (Table 5). Patients with baseline CD4 > 200 had higher crude suppression than those with CD4 ≤ 200 (61.3% vs. 46.1%), and in the adjusted model they had lower odds of non-suppression (aOR = 0.53, 95% CI: 0.40–0.70; $p < 0.001$), which is equivalent to approximately 1.89-fold higher odds of being suppressed. In contrast, clinic type, sex, age, and WHO clinical stage were not independently associated with suppression. Suppression was slightly higher at clinics than CHCs (57.3% vs. 54.6%), but CHC care was not associated with non-suppression after adjustment. Females had a higher crude suppression proportion than males (58.5% vs. 50.9%); however, the adjusted association was borderline and not statistically significant (aOR = 0.75, 95% CI: 0.55–1.01; $p = 0.055$). Suppression was similar by age group (≤ 34 years: 55.7% vs. > 34 years: 56.2%; aOR = 0.82, 95% CI: 0.62–1.09; $p = 0.164$). Patients initiating ART at WHO Stage III–IV had lower crude suppression than those at Stage I–II (52.3% vs. 57.2%), but the adjusted association was not significant (aOR = 0.93, 95% CI: 0.67–1.28; $p = 0.645$).

Discussion

This study examined long-term treatment outcomes over a 10-year period among PLWHIV who initiated ART in 2013 in Tshwane District, South Africa. The primary outcomes retention in care, mortality, and viral suppression, were significantly influenced by age, gender, clinical stage at initiation, and type of health facility attended. These findings underscore the importance of differentiated care approaches that account for demographic and clinical heterogeneity among patients to improve long-term HIV outcomes. Overall, retention in care after 10 years was 47.7%, with 30.4% LTF, 20.1% transferred out, and 3.3% deceased. Kaplan–Meier curves highlighted that attrition was most pronounced within the first two years, particularly among younger adults, underscoring the vulnerability of early treatment engagement. These findings are comparable to other long-term ART cohort studies in sub-Saharan Africa, where retention beyond five years often falls below 50%.[9] Despite expanded ART access, long-term retention remains a substantial challenge, especially given the programmatic shift from earlier "test and treat" models to long-term chronic care frameworks.

Kaplan–Meier analysis revealed that younger adults, particularly those aged 18–24 years, experienced the steepest early declines in retention, highlighting their vulnerability to loss to follow-up. These findings align with global and regional studies demonstrating that young adults face unique barriers to sustained care, including stigma, mobility, competing life priorities, and lower health literacy [4, 8]. Conversely, older participants (>34 years) had better retention but significantly higher mortality. This may reflect a survivor effect among younger participants or the presence of comorbidities and delayed treatment initiation in older adults [10]. Importantly, mortality was highest among those aged 34 years and older and was strongly associated with advanced WHO clinical staging at ART initiation. Patients initiating ART at WHO Stage IV had markedly poorer survival, with the Kaplan–Meier curves showing the steepest and earliest declines, and Cox regression confirming a more than threefold increased risk of death compared to those in Stage I. This finding is consistent with previous studies linking late-stage HIV diagnosis to poor long-term prognosis.[11]

Two-thirds of the cohort were female, reflecting regional patterns of the epidemic. Women demonstrated greater immunologic recovery than men in our data, which is consistent with reviews reporting faster immunovirologic response among women on ART [12]. Despite this, sex was not an independent predictor of retention, mortality, or viral suppression after adjustment in our models; this aligns with a prior systematic review showing women's survival advantage over men without consistent differences in virologic or immunologic endpoints across studies [13]. At the same time, multiple systematic reviews document higher mortality among men on ART in low- and middle-income settings and persistent gaps in the male engagement/retention context that likely reflect later presentation and social/structural barriers [14, 15].

Facility type emerged as an important determinant of long-term outcomes in this cohort. Patients managed at CHCs demonstrated significantly better CD4 recovery, higher retention in care, and lower mortality compared to those receiving care at clinics. This may reflect differences in resource allocation, staffing, or availability of services at CHCs, which often provide more integrated and comprehensive care [16]. While clinics serve as critical points of care, enhancing their capacity to offer continuous and high-quality HIV care could contribute to improved long-term outcomes.

Immunological status at baseline, as reflected by CD4 counts, was an important predictor of viral suppression. Participants who initiated ART with CD4 > 200 cells/μL were younger, had better immune recovery, and were more likely to suppress viral loads compared to those with lower baseline CD4. These findings reinforce current WHO guidelines advocating for early ART initiation irrespective of CD4 count, given the clear benefits of preserving immune function. While CD4 count at ART initiation was not significantly associated with mortality in linear regression analysis, likely due to confounding with WHO staging, the strong correlation between higher CD4 change at follow-up and viral suppression supports CD4 monitoring as a relevant program indicator.

Our findings demonstrate that patients presenting with advanced HIV disease (WHO Stage III/IV) had a significantly higher hazard of death compared to those in early stages, with the survival curves showing steeper and earlier declines. This aligns with long-standing evidence that late-stage initiation of ART is one of the strongest predictors of poor prognosis, reflecting advanced immune suppression, higher opportunistic infection burden, and delayed linkage to care [17]. Importantly, advanced staging is not only a clinical marker but also a health system signal of gaps in HIV testing, delayed diagnosis, and late linkage to care. Despite expansion of ART eligibility and "test-and-treat" policies, a considerable proportion of patients in many African settings still initiate therapy at advanced stages [17]. Our results reinforce that strengthening community-based HIV testing, improving linkage pathways, and early initiation of ART remain essential strategies to reduce late presentation.

From a programmatic perspective, our findings highlight key areas for targeted interventions. Young adults require differentiated models of care that address their unique developmental, social, and economic needs such as youth-friendly clinics, mental health integration, and

flexible clinic hours. For older adults, especially those with comorbidities, comprehensive screening and management of non-communicable diseases (NCDs) are essential to improve survival. Gender-responsive programming must also be prioritized, with male-focused community testing campaigns and stigma reduction strategies to increase men's engagement in care.

The strengths of this study include its large sample size, use of routinely collected Tier.Net data, and 10-year follow-up period. However, limitations should be acknowledged. First, reliance on routine data may introduce misclassification or underreporting of outcomes such as death, especially in patients lost to follow-up. Second, we were unable to assess socio-economic variables or behavioral factors due to data limitations. No active tracing was performed to verify outcomes; retention status was based on Tier.Net records, which may have led to misclassification in cases where patients re-engaged in care elsewhere. As some participants may have been lost and later re-engaged, the latter outcome was used; hence, Cox regression estimates of LTFU should be interpreted with caution. Finally, while viral load suppression was analyzed, adherence measures were not included, which could provide further insight into long-term treatment success.

Conclusion

This study provides critical insights into long-term ART outcomes in a real-world public sector setting. Retention in care remained suboptimal at less than 50% after a decade, with the steepest attrition occurring in the first two years, particularly among younger adults. Mortality was strongly predicted by older age and advanced WHO staging at initiation, highlighting the persistent consequences of late presentation to care. Patients managed at CHCs demonstrated superior outcomes across CD4 recovery and survival compared to those at clinics, underscoring the value of differentiated service delivery models. Baseline immunological status also influenced long-term viral suppression, reinforcing the importance of early ART initiation before significant immune decline.

Taken together, these findings emphasize the need for targeted, age- and gender-responsive interventions, expansion of community-based HIV testing, and strengthening of clinic capacity to provide comprehensive care. Sustained improvements in HIV outcomes in South Africa will require addressing structural barriers to early diagnosis and retention, optimizing differentiated models of service delivery, and integrating broader health system responses, including the management of comorbidities in older patients.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12981-025-00814-9.

Additional file 1.

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Author contributions

Kateko Mhlongo (KM) conceptualized the study, collected and analyzed the data, and drafted the initial manuscript.Dr. Sanele Ngcobo (SN) supervised the study, guided the methodological design, contributed to interpretation of the findings, and critically revised the manuscript for important intellectual content.ML Murray Louw (ML) assisted with statistical analysis and contributed to proofreading and refinement of the manuscript.

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Data availability

The dataset used and analyzed during the current study is available from the corresponding author upon reasonable request and in accordance with institutional and district data-sharing policies.

Data availability

The dataset used and analyzed during the current study is available from the corresponding author upon reasonable request and in accordance with institutional and district data-sharing policies.

Declarations

Ethics approval and consent to participate

This study was approved by the University of Pretoria Faculty of Health Sciences Research Ethics Committee (Reference: 342/2024) and the Tshwane District Health Research Committee. As this was a retrospective cohort study using de-identified secondary data from Tier.Net, a waiver of informed consent was granted by both ethics committees. No participants were contacted or recruited for the study.

Consent for publication

Not applicable. This study involved the analysis of de-identified, routinely collected secondary data from the Tier.Net system. No individual-level identifiable information (such as names, photographs, or personal narratives) was included in the manuscript. Therefore, individual consent to publish was not required.

Competing interests

The authors declare no competing interests.

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